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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,500	11/21/2003	Joseph Chappell	8064-005-CIP-2	8924

32301 7590 09/30/2008

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	PAPER NUMBER
1638	
MAIL DATE	DELIVERY MODE
09/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,500	CHAPPELL ET AL.	
	Examiner	Art Unit	
	RUSSELL KALLIS	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/02/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 20-23 are newly added, claims 10-23 are pending and examined

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 10-19 remain and new claims 20-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION. This rejection is maintained for the reasons of record set forth in the Official action mailed 3/06/2008. Applicant's arguments filed 7/2/2008 have been considered but are not deemed persuasive.

Applicant asserts that there is support for "at least one isoprenoid reaction product . . ." recited in line 5 of claim 10, and "more than one isoprenoid reaction product in a ratio differing from the ratio of the products produced in the absence of the second isoprenoid synthase polypeptide" recited in lines 7-8 of claim 10, because the specification "clearly and unequivocally" states at page 4 lines 5-9 that the chimeric isoprenoid synthase is capable of catalyzing the production of isoprenoid products that are not produced in the absence of the second domain of the second, heterologous isoprenoid synthase (response pages 9-10). Further, with respect to Applicant's remarks showing support in the specification for the language of claim 10 section (2), all of those portions of the specification to which Applicants refer all recite domains of first or second isoprenoid synthase polypeptides which is narrower in scope than the

instant claim 10 limitations. Applicant's amendment is broader in scope than the invention contemplated in the specification; and thus constitutes new matter. Moreover, there is no support in the figurers or specification for "produced in the absence", the specification only supports "not produced in the absence".

Claims 10-19 remain and new claims 20-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 12/13/2006, 7/12/2007, and 3/06/2008. Applicant's arguments filed 7/2/2008 have been considered but are not deemed persuasive.

Applicant asserts that an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, they were in possession of the invention and that the claims now have specific language that recites domains involved in the chimeric proteins and relevant identifying characteristics such that there is sufficient structural and functional detail (response pages 11-14).

Applicants' amendments to the claims recite in claim 10 a sesquiterpene synthase and in claim 20 a DDXXD motif. However, the examples provided by Applicant in the specification do not clearly describe the broadly claimed generic invention of the instant claims because there are insufficient relevant identifying characteristics.

Applicant asserts on page 19 that U.S. Patent 5,824,774 shows novel enzymes capable of synthesizing new reaction products is incorrect. There is no mention of new reaction products in

the claims or any reduction to practice of new reaction products taught in the specification. Applicant is therefore unable to name specifically those reaction products that are novel.

A summation of Applicants arguments from pages 20-23 of the response is that the product specificity domains comprised within exons 4 and 6 of wild type tobacco and henbane sesquiterpene synthase enzymes respectively together with the ratio domain DDXXD define Applicants' genus of chimeric sesquiterpene synthases, and that one of ordinary skill would be able to identify other chimeric sesquiterpene synthases.

Applicant asserts that knowledge of the identity of the products formed by the enzymes would not have any relevance to the issue of written description because the claims are directed to nucleic acid constructs (response page 24).

Applicant asserts that it is not required to recite each and every domain of the claimed chimeras (response page 25). Applicant has not recited in the claims the identity of any domain of the chimeric proteins other than the DDXXD ratio domain of claims 20-23; and thus Applicant has not defined the relevant characteristics of the claimed nucleic acid structure or the protein encoded therein.

Applicant asserts that the work of Schalk and Croteau PNAS 2000; pp. 11948-11953; demonstrates post filing evidence for chimeric enzymes generated by a domain swapping process (page 26 response). This is not made evident by Schalk *et al.* (PNAS, 97; (22): pp. 11948-11953), where the author's remarks are directed towards the involvement of specific residues and the importance of progressively placed directed mutations into a conserved region and not asymmetrically positioned domains as being determinant for changes in product formation. Further, the swapping of portions of the two respective enzymes analyzed by Schalk *et al.* did

not follow recognized intron exon boundaries but rather were determined as a matter of conveniently located restriction sites within the cDNA. Moreover, the publication date of the cited reference is well after the date of the priority claim (4/12/1996) of the instant application and does not support Applicant's assertion that the reference provides a description of the broadly claimed genus of chimeric isoprenoid synthase polypeptides and polynucleotides encoding said polypeptides. Furthermore, the work of Schalk and Croteau did not result in the formation of a ratio of products of the two hydroxylases.

With respect to Applicants' remarks directed to the Dudareva reference it is acknowleged that the claims are now directed to sesquiterpene synthases.

Claims 10-19 remain and new claims 20-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule encoding a chimeric isoprenoid synthase polypeptide selected from the group consisting of (a) the tobacco-Hyoscyamus CH4 chimeric isoprenoid synthase; (b) the tobacco-Hyoscyamus CH10 chimeric isoprenoid synthase; (c) the tobacco-Hyoscyamus CH11 chimeric isoprenoid synthase; (d) the tobacco-Hyoscyamus CH12 chimeric isoprenoid synthase; (e) the tobacco-Hyoscyamus CH13 chimeric isoprenoid synthase; and (f) the tobacco-Hyoscyamus CH14 chimeric isoprenoid synthase; and vectors thereof, and plant cells and plants transformed therewith, does not reasonably provide enablement for DNA encoding a chimeric isoprenoid sesquiterpene synthase polypeptide, wherein said chimeric isoprenoid synthase polypeptide comprises a first isoprenoid synthase polypeptide joined to a second different isoprenoid synthase polypeptide such that the chimeric isoprenoid sesquiterpene synthase polypeptide encoded by the DNA catalyzes: (I) the production of at least one isoprenoid reaction product that is not produced in the absence of the

second isoprenoid synthase polypeptide; or (2) the production of more than one isoprenoid reaction product in a ratio differing from the ratio of the products produced in the absence of the second isoprenoid synthase polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicants' arguments with respect to enablement are largely directed to the argument that experimentation would be required and that what is largely known can be omitted from the specification and if predictability can be minimized by the knowledge in the art (response pages 23-27); see See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention. Moreover, the structure of the broad genus of isoprenoid sesquiterpene synthases and their respective functions are not largely known and would require undue trial and error experimentation.

With respect to Applicants' remarks directed to the Dudareva reference it is acknowleged that the claims are now directed to sesquiterpene synthases.

In addition, since the publication dates of the cited reference Schalk and Croteau PNAS, are well after the date of the claimed priority (4/12/1996) of the instant application the references show that the state of the art did not and still does not support Applicant's broad claim to chimeric isoprenoid sesquiterpene synthases; and contradict Applicant's assertions that the prior art and the relative skill of those in the art provide enablement for making and using the broadly claimed genus of chimeric isoprenoid sesquiterpene synthase polypeptides or provide evidence

that the degree of unpredictability is overcome by one of ordinary skill because the work of Schalk and Croteau did not result in the formation of a ratio of products of the two hydroxylases.

Applicant asserts that the Office has not met the burden of countering the actual examples in the specification. Those specific examples are not rejected. Rather the lack of examples is what forms the basis of the rejection and that there is no teaching in the art or Applicants' specification to support the broadly claimed genus.

Applicants' assertions on pages 38-44 are have either been addressed in a previous office action or addressed supra.

Given the unpredictability in the art as to which domains from which plants would tolerate chimerization and produce at least a bifunctional enzyme; the breadth of the claims encompassing any plant cell comprising any number of enzymatic domains selected from a broad category of unspecified isoprenoid sesquiterpene synthases; the lack of guidance in the specification or in the prior art as to which domains of the isoprenoid sesquiterpene synthase enzyme family would best serve the invention; one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictably eliminated. Thus, undue trail and error experimentation would be needed to make and clone a multitude of non-exemplified isoprenoid sesquiterpene synthase chimeras and to test them in a myriad of non-exemplified expression systems for a multitude of non-exemplified isoprenoid sesquiterpene products. Therefore, the invention is not enabled for the full scope of the claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Russell Kallis/
Primary Examiner, Art Unit 1638
September 23, 2008